IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re the application of:	)	Group Art Unit: 1642
	)	
TALOR	)	Examiner: Gary B. Nickol
	)	
Serial No. 10/611,914	)	
	)	
Filed: July 03, 2003	)	

For: **A METHOD OF PRE-SENSITIZING CANCER PRIOR TO TREATMENT WITH RADIATION AND/OR CHEMOTHERAPY AND A NOVEL CYTOKINE MIXTURE**

Appendix B

Please amend the claims according to the July 30, 2003, revision to 37 C.F.R. § 1.121 concerning a manner for making claim amendments.

1. (Original) A method for pre-sensitizing cancer prior to a therapeutic treatment, comprising the step of:

administering a therapeutically active amount of a serum-free and mitogen-free cytokine mixture to cancer.

2. (Original) The method of claim 1, wherein said therapeutic treatment is selected from the group consisting of chemotherapy, immuno-therapy and radiation therapy.

3. (Original) The method of claim 1, wherein said serum-free and mitogen-free cytokine mixture is peritumorally administered three times a week over a two week period in a range from about 20 IU to 1600 IU wherein IU represent International Units for Interleukin-2 given in World Health Organization 1st International Standard for Human IL-2, 86/504.

4. (Original) The method of claim 1, wherein said serum-free and mitogen-free cytokine mixture is peritumorally administered three times a week over a two week period in a range from about 40 IU to 800 IU wherein IU represent International Units for Interleukin-2 given in World Health Organization 1st International Standard for Human IL-2, 86/504.

5. (Original) The method of claim 1, wherein said serum-free and mitogen-free cytokine mixture is peritumorally administered three times a week over a two week period in a range from about 35 IU to 75 IU

wherein IU represent International Units for Interleukin-2 given in World Health Organization 1st International Standard for Human IL-2, 86/504.

6. (Original) The method of claim 1, wherein said serum-free and mitogen-free cytokine mixture is peritumorally administered three times a week over a two week period at 55 IU wherein IU represent International Units for Interleukin-2 given in World Health Organization 1st International Standard for Human IL-2, 86/504.

7. (Original) The method of claim 1, wherein said serum-free and mitogen-free cytokine mixture is peritumorally administered three times a week over a two week period at 400 IU wherein IU represent International Units for Interleukin-2 given in World Health Organization 1st International Standard for Human IL-2, 86/504.

8. (Original) The method of claim 1, wherein said serum-

free and mitogen-free cytokine mixture is peritumorally administered three times a week over a two week period at 800 IU wherein IU represent International Units for Interleukin-2 given in World Health Organization 1st International Standard for Human IL-2, 86/504.

9. (Original) The method of claim 1, wherein said serum-free and mitogen-free cytokine mixture is peritumorally administered five times a week over a two week period at 800 IU wherein IU represent International Units for Interleukin-2 given in World Health Organization 1st International Standard for Human IL-2, 86/504.

10. (Original) The method of claim 1, wherein said serum-free and mitogen-free cytokine mixture is comprised of specific ratios of cytokines selected from the group of IL-1β, TNF-α, IFN-γ and GM-CSF to Interleukin-2 (IL-2) as follows:

IL-1β to IL-2 at a ratio range of 0.4 - 1.5;

TNF-α to IL-2 at a ratio range of 3.2 - 10.9;

IFN-γ to IL-2 at a ratio range of 1.5 - 10.9; and

GM-CSF to IL-2 at a ratio range of 2.2 - 4.8.

11. (Original) The method of claim 10, wherein said specific ratios of cytokines are as follows:

IL-1β to IL-2 at a ratio range of 0.6 to 0.8;

TNF-α to IL-2 at a ratio range of 7.7 to 11.3;

IFN-γ to IL-2 at a ratio range of 4.9 to 7.1; and

GM-CSF to IL-2 at a ratio range of 3.5 to 4.5.

12. (Original) The method of claim 1 wherein the serum-free and mitogen-free cytokine mixture is Multikine®.

13. (Original) A method for inducing tumor cells into a cell cycle selected from the group of G_1, S, G_2 and M , comprising the step of:

administering a therapeutically active amount of a serum-free and mitogen-free cytokine mixture to a cancerous cell.

14. (Original) The method of claim 13, wherein said serum-free and mitogen-free cytokine mixture is peritumorally administered three times a week over a two week period in a range from about 20 IU to 1600 IU wherein IU represent International Units for Interleukin-2 given in World Health Organization 1st International Standard for Human IL-2, 86/504.

15. (Original) The method of claim 13, wherein said serum-free and mitogen-free cytokine mixture is peritumorally administered three times a week over a two week period in a range from about 40 IU to 800 IU wherein IU represent International Units for Interleukin-2 given in World Health Organization 1st International Standard for Human IL-2, 86/504.

16. (Original) The method of claim 13, wherein said serum-free and mitogen-free cytokine mixture is peritumorally administered three times a week over a two week period in a range from about 35 IU to 75 IU wherein IU represent International Units for

Interleukin-2 given in World Health Organization 1st International Standard for Human IL-2, 86/504.

17. (Original) The method of claim 13, wherein said serum-free and mitogen-free cytokine mixture is peritumorally administered three times a week over a two week period at 55 IU wherein IU represent International Units for Interleukin-2 given in World Health Organization 1st International Standard for Human IL-2, 86/504.

18. (Original) The method of claim 13, wherein said serum-free and mitogen-free cytokine mixture is peritumorally administered three times a week over a two week period at 400 IU wherein IU represent International Units for Interleukin-2 given in World Health Organization 1st International Standard for Human IL-2, 86/504.

19. (Original) The method of claim 13, wherein said serum-free and mitogen-free cytokine mixture is

peritumorally administered three times a week over a two week period at 800 IU wherein IU represent International Units for Interleukin-2 given in World Health Organization 1st International Standard for Human IL-2, 86/504.

20. (Original) The method of claim 13, wherein said serum-free and mitogen-free cytokine mixture is peritumorally administered five times a week over a two week period at 800 IU wherein IU represent International Units for Interleukin-2 given in World Health Organization 1st International Standard for Human IL-2, 86/504.

21. (Original) The method of claim 13, wherein said serum-free and mitogen-free cytokine mixture is comprised of specific ratios of cytokines selected from the group of IL-1β, TNF-α, IFN-γ and GM-CSF to Interleukin-2 (IL-2) as follows:

IL-1β to IL-2 at a ratio range of 0.4 - 1.5;

TNF-α to IL-2 at a ratio range of 3.2 - 10.9;

IFN-γ to IL-2 at a ratio range of 1.5 - 10.9; and

GM-CSF to IL-2 at a ratio range of 2.2 - 4.8.

22. (Original) The method of claim 21, wherein said specific ratios of cytokines are as follows:

IL-1β to IL-2 at a ratio range of 0.6 to 0.8;

TNF-α to IL-2 at a ratio range of 7.7 to 11.3;

IFN-γ to IL-2 at a ratio range of 4.9 to 7.1; and

GM-CSF to IL-2 at a ratio range of 3.5 to 4.5.

23. (Original) The method of claim 13 wherein the serum-free and mitogen-free cytokine mixture is Multikine®.

24. (Original) A serum-free and mitogen-free cytokine mixture, comprising specific ratios of cytokines selected from the group of IL-1β, TNF-α, IFN-γ and GM-CSF to Interleukin-2 (IL-2) as follows:

IL-1β to IL-2 at a ratio range of 0.4 - 1.5;

TNF-α to IL-2 at a ratio range of 3.2 - 10.9;

IFN-γ to IL-2 at a ratio range of 1.5 - 10.9; and

GM-CSF to IL-2 at a ratio range of 2.2 - 4.8.

25. (Original) The serum-free and mitogen-free cytokine mixture of claim 24, wherein said specific ratios of cytokines are as follows:

IL-1β to IL-2 at a ratio range of 0.6 to 0.8;

TNF-α to IL-2 at a ratio range of 7.7 to 11.3;

IFN-γ to IL-2 at a ratio range of 4.9 to 7.1; and

GM-CSF to IL-2 at a ratio range of 3.5 to 4.5.

26. (Currently Amended) A pharmaceutical composition for use in treating cancer, comprising specific ratios of cytokines selected from the group of IL-1β, TNF-α, IFN-γ and GM-CSF to Interleukin-2 (IL-2) as follows:

IL-1β to IL-2 at a ratio range of 0.4 - 1.5;

TNF-α to IL-2 at a ratio range of 3.2 - 10.9;

IFN-γ to IL-2 at a ratio range of 1.5 - 10.9;

GM-CSF to IL-2 at a ratio range of 2.2 - 4.8, and optionally in combination with a pharmaceutically acceptable excipient, carrier or additive [[.]] .

27. (Original) The pharmaceutical composition of claim 26,

wherein said specific ratios of cytokines are as follows:

IL-1β to IL-2 at a ratio range of 0.6 to 0.8;

TNF-α to IL-2 at a ratio range of 7.7 to 11.3;

IFN-γ to IL-2 at a ratio range of 4.9 to 7.1; and

GM-CSF to IL-2 at a ratio range of 3.5 to 4.5.

28. (Original) The pharmaceutical composition of claim 27, further comprising an IL-3 to IL-2 ratio in a range from 0.38 - 0.68, preferably at 0.53+/- 0.15

29. (Original) The pharmaceutical composition of claim 27, further comprising an IL-6 to IL-2 ratio in a range from 37.2 - 53.8, preferably at 46+/- 5.9.

30. (Currently Amended) The pharmaceutical composition of claim 27, further comprising an IL-8 to IL-2 ratio in a range from 261 - 561.5, preferably at ~~41~~ 411 +/- 10.6.

31. (Original) The pharmaceutical composition of claim 27,

further comprising an IL-1α to IL-2 ratio in a range from 0.56 - 0.94, preferably at 0.75+/- 0.19.

32. (Currently Amended) The pharmaceutical composition of claim 27, further comprising an IL-10 to IL-2 ratio in a range from ~~2.87~~ 2.82 - 3.22, preferably at 3.0+/- 0.18.

33. (Currently Amended) The pharmaceutical composition of claim 27, further comprising an IL-16 to IL-2 ratio in a range from ~~1.24~~ 1.16 - 2.84, preferably at 1.84+/- 0.68.

34. (Original) The pharmaceutical composition of claim 27, further comprising a G-CSF to IL-2 ratio in a range from 2.16 - 3.78, preferably at 2.97+/- 0.81.

35. (Currently Amended) The pharmaceutical composition of claim 27, further comprising a TNF-β to IL-2 ratio in a range from ~~1.18~~ 1.17 - 2.43, preferably at 1.8+/- 0.63.

36. (Currently Amended) The pharmaceutical composition of claim 27, further comprising a MIP-1α to IL-2 ratio in a range from ~~16.78~~ 15.7 - 37.16, preferably at 22.7+/- 7.0.

37. (Currently Amended) The pharmaceutical composition of claim 27, further comprising a MIP-1β to IL-2 ratio in a range from ~~19.2 - 26.4~~ 17.1-28.5, preferably at 22.8+/- 5.7.

38. (Original) The pharmaceutical composition of claim 27, further comprising a RANTES to IL-2 ratio in a range from 2.3 - 2.7, preferably at 2.5+/- 0.13.

39. (Currently Amended) The pharmaceutical composition of claim 27, further comprising a EGF to IL-2 ratio in a range from ~~0.27 - 0.28~~ 0.267 - 0.283, preferably at 0.275+/- 0.008.

40. (Currently Amended) The pharmaceutical composition of

claim 27, further comprising a PGE_2 to IL-2 ratio in a range from ~~3.68~~ 3.63 - 5.42, preferably at 4.5+/- 0.87.

41. (Currently Amended) The pharmaceutical composition of claim 27, further comprising a TxB_2 to IL-2 ratio in a range from ~~23.5 - 25.1~~ 23.47 - 25.13, preferably at 24.3+/- 0.83.